

**DENTINO**  
**JURNAL KEDOKTERAN GIGI**  
**Vol IX. No 1. March 2024**

**TETRACYCLINE MOUTHWASH AS ORAL CAVITY ULCER THERAPY IN PATIENTS WITH A HISTORY OF ALLERGIES**

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**ABSTRACT**

**Background:** One of the allergic reactions in the oral mucosa is ulceration caused by IgE-mediated reactions to food substances or non-IgE-mediated reactions and non-immunological mechanisms. Ulceration is a damage to the epithelium of the oral cavity that affects the nerve endings in the lamina propria layer so that it causes pain or heat that requires treatment and therapy. **Objective:** To report the occurrence of ulcers due to food allergies and therapy with tetracycline mouthwash 0.25% solution. **Case:** A 22-year-old female patient came with complaints of a small ulcer on the inside of the gums and the entire upper and lower lips and a numb and dry tongue. The patient always experiences an ulcer every time he eats seafood and certain foods that the patient cannot mention because it happens so often and every time an ulcer appears it will continue to get bigger. **Management:** Patients are advised to avoid allergens and refer for a complete blood allergy test and Ig E. Tetracycline mouthwash 0.25% solution was given to be rinsed three times a day. And added supportive therapy, giving multivitamins. **Conclusion:** Tetracycline mouthwash has antimicrobial properties and properties as inhibitors of tissue metalloproteinases (TIMPs) can accelerate healing time and ulceration does not continue to get bigger, reduce taste and pain, according to the theory it can reduce secondary speed limits and duration. inhibits collagenase.

**Keyword:** Allergy, Mouthwash, Tetracycline, Ulcer

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**INTRODUCTION**

Ulceration is damage to the oral cavity epithelium that affects the nerve endings in the lamina propria layer, causing pain or burning, especially when eating spicy or sour foods. In general, patients experience various complaints about burning and pain related to ulceration in the oral cavity.<sup>1,2,3</sup> Oral ulcers can be caused by various things, including trauma, immunological disorders, defects in the immune system, infections, cancer, malnutrition and gastrointestinal diseases.<sup>2,4</sup> Apart from that, allergies are also one of the causes of ulceration in the oral cavity, usually caused by allergies to food, drugs, cosmetics, metals, toothpaste, dental materials and microorganisms.<sup>5</sup>

Symptoms and features of allergies caused by food vary greatly from small papules, plaques, vesicles, ulceration or edema to life-threatening conditions (fatal anaphylaxis), mostly affecting the skin, gastrointestinal tract and upper and lower respiratory tract. Each individual also has differences in allergens that cause allergic reactions.<sup>2,5</sup>

The healing of an ulcerated lesion in the oral cavity is influenced by various things. Appropriate therapy really helps patients feel more comfortable. Tetracycline is a broad spectrum antibiotic that has good activity against most gram-negative and positive bacteria, and has more activity and killing power due to its pharmacokinetic properties. Tetracycline mouthwash has potential as a therapy for oral ulceration.<sup>6,7</sup> Based on the above, the aim of this case report is to report the effectiveness of using tetracycline mouthwash in patients with a history of food allergies.

**CASE**

On July 2nd, 2019, a 22 year old female patient came to the Oral Medicine Clinic of the Dental and Oral Department of RSAL Dr. Ramelan with complaints that there were small ulcer sores on the inner gums and the entire upper and lower lips and tongue felt numb and dry. Ulcer sores appeared three days ago for no apparent reason and hurt when eaten. The numbness that occurred in the lips and tongue occurred the day before after the patient ate squid.

The patient always experiences mouth ulcers every time he eats seafood and certain foods which the patient cannot name because they occur very often and every time an ulcer appears it will continue to get bigger. Since the age of 13, the patient has been diligently going to the dentist to treat his teeth and his allergic complaints, but until now the patient has not received satisfactory therapy. The patient has a history of seafood allergies, however the patient has a hobby of eating seafood and almost always refuses to consume it even though it results in ulcer sores. Family history indicated that the patient's mother also suffered from food allergies. The patient has never had an allergy test.

Based on intra-oral examination, it was found that the labial mucosa of the upper and lower jaw, tongue, and buccal mucosa looked reddish, felt numb (thick), uncomfortable, painless (painful). On the inner mandibular gingiva (lingual aspect) there is an oval ulcer with a diameter of 2 mm, painful, with a white base with reddish edges of the lesion.

Extraoral examination revealed that the left and right submandibular glands were palpable, soft and slightly painful.

## CASE MANAGEMENT

### Visit I (2nd July 2019)

At the initial visit, from the history and clinical examination, this case was tentatively diagnosed as allergic stomatitis with a differential diagnosis of recurrent aphthous stomatitis. Patients are advised to avoid allergens and are referred for allergy, complete blood count and IgE tests.

Mouthwash tetracycline solution 0.25% is given to gargle three times a day. And added supportive therapy, multivitamins containing Vit B1 50 mg, Vit B2 25 mg, Vitamin B6 10 mg, Vitamin B12 5 mcg, Vitamin C 500 mg, niacinamide 50 mg, Ca pantothenate 20 mg.

The patient was advised to undergo control on July 6 by bringing the results of allergy tests, complete blood count and IgE.



Figure 1 Visit 1. Lip mucosa that appears erythematous

### Visit II (6th July 2019)

The patient came on the 4th day, the patient submitted the results of a complete blood test which showed an Hb of 13.4 g/dl; Leukocytes 9 k/ $\mu$ L; platelets 366 thousand/ $\mu$ L; Eosinophils 4%; Basophils 2%; Segment 69%; Lymphocytes 24%; monocytes 1% and ESR 15%.

The patient informed that tetracycline mouthwash was used regularly, the numbness in the mouth had reduced, only remaining on the tip of the lower lip, but more and more ulceration appeared on the lower lip, left buccal mucosa and lateral tongue. The patient also explained that he was currently facing a final exam.

Intra-oral examination revealed multiple small ulcers on the lower lip mucosa (6) with an average diameter of 0.5 to 1 mm, on the left lateral side of the tongue there were multiple small ulcers (4) with an average diameter of 0.5 mm and on the mucosa. The left buccal also showed multiple small ulcers (3) with an average diameter of 0.5 mm with a white base and reddish and painful edges. Extraoral examination revealed that the left and right submandibular glands were palpable, soft and slightly painful.

Patients were instructed to continue therapy with tetracycline mouthwash, optimize oral hygiene and avoid foods suspected to be allergens. Patients are advised to have control on July 9th, 2019.

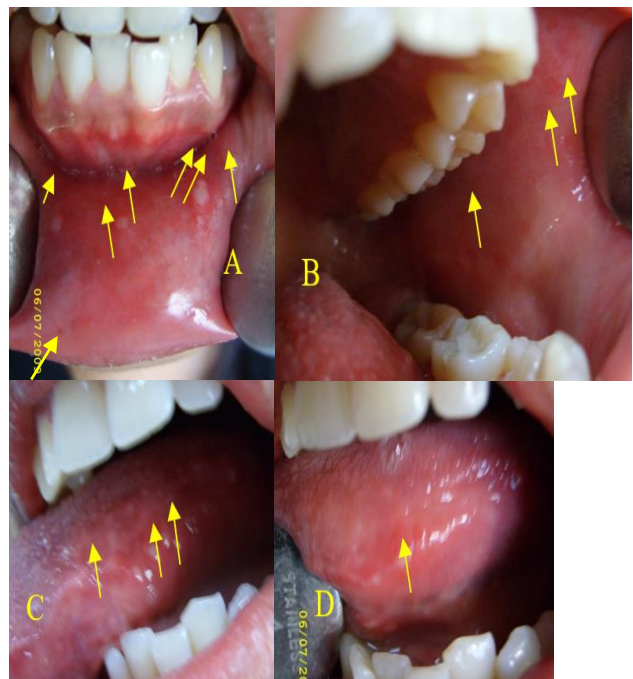


Figure 2 Visit 2. Multiple small ulcers (6 pieces) with an average diameter of 0.5 to 1 mm (A). The left buccal mucosa also had multiple small ulcers (3 pieces) with an average diameter of 0.5 mm (B) lateral to the left tongue there are multiple small ulcers (4 pieces) with an average diameter of 0.5 mm (C & D)

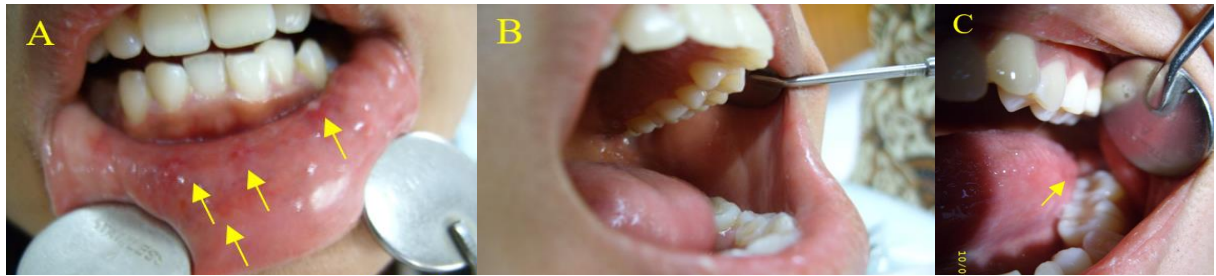


Figure 3 Visit 3. shallow ulcers, multiple (4 pieces), diameter 0.5 mm (A) left buccal mucosa no longer found ulcers (B) left lateral tongue there is a painless single shallow ulcer diameter 0.5 mm, white base and there is erythematous at the margin of the ulcer (C)

### Visit III (10th July 2019)

The patient came on the 8th day, one day later than scheduled, this was because the patient was busy taking the UAS. The patient explained that the mouthwash was still being used according to the rules and routine, the ulcer sores had healed, and they no longer felt painful. The numbness in the patient's mouth has healed so that the patient can eat and drink comfortably again. The IgE examination results were: 474.6.

Intraoral examination, on the lower lip, there were shallow ulcers, multiple (4), 0.5 mm in diameter and on the left lateral side of the tongue there was a single shallow ulcer with a diameter of 0.5 mm, painless, white base and there was redness at the edge of the ulcerated lesion. The ulcer is in the healing phase. Extra oral examination showed that the upper and lower lips looked dry.

Patients are instructed to continue mouthwash therapy, optimize oral hygiene and avoid foods that are suspected to be allergens. The patient was instructed for control on July 15th, 2019.



Figure 4 Visit 4. All ulcers have healed

### Visit IV (15th July 2019)

IV visit on the 13th day, the patient has stopped mouthwash therapy since July 12nd, 2019 because the ulcer sores have healed, are painless, and the numbness has also disappeared. Patients can eat and drink comfortably.

Intraoral examination shows that the entire oral cavity mucosa is normal, all ulcers have healed, as well as extra oral examination it appears that the upper lip is no longer dry, the

submandibular glands also no longer feel painful when palpated. Allergy test results show the patient is allergic to several allergens (allergy test results attached). The patient was declared cured and therapy was stopped.

### DISCUSSION

Food allergy is a collection of symptoms that affect many organs and body systems caused by food allergies. In some literature, food allergy is used to express a reaction to food which is basically a type I hypersensitivity reaction and hypersensitivity to food which is basically a type III and IV hypersensitivity reaction (Olifier 2013). Food allergy is also a condition caused by an IgE-mediated reaction to food substances. On the other hand, reactions to food can be non-IgE-mediated and non-immunologic mechanisms.<sup>8</sup>

The immune mechanisms underlying reactions in the skin and mucosa include IgE-mediated, cell-mediated (non-IgE-mediated) and mixed cellular reactions. Meanwhile, non-immunological mechanisms, for example reactions due to irritants, toxic substances or the presence of something non-specific in food, currently the prevalence of food allergies is increasing.<sup>8</sup> One form of allergic reaction to the oral mucosa is ulceration, where allergens contained in food are absorbed in the ileum and circulate throughout the body systemically, causing the pathogenesis of allergic stomatitis when they infiltrate the oral mucosa.<sup>2</sup> In this case, the complete blood examination did not show any abnormal conditions, except for eosinophils which were seen at the upper limit and the IgE examination showed a very high increase in the value (474.6 normal value < 100) and the prick test also showed that the patient was hypersensitive to several type of allergen, indicating that the patient does have hypersensitivity to several types of food.

Ulceration in the oral cavity which causes damage to the oral cavity epithelium

affects the nerve endings in the lamina propria layer, causing pain or burning, especially when eating spicy or sour foods. This really disturbs the patient's activities and comfort.<sup>4</sup> This requires treatment and therapy that can help the patient to be able to function properly again.

This case uses a mouthwash, tetracycline solution 0.25%, which is given to gargle three times a day. Tetracycline is a broad spectrum bacteriostatic antibiotic that works to inhibit protein synthesis in bacteria. This antibiotic is effective against gram-negative and positive bacteria. Tetracyclines enter microorganisms via passive diffusion or by active transport that uses energy. This drug works intracellularly and after entering also binds reversibly to the bacterial ribosome 30S subunit, closing the aminoacyl-tRNA bond to the acceptor site in the mRNA-ribosome complex, which prevents amino acids from forming peptides.<sup>9</sup> Administering tetracycline mouthwash helps control bacteria in the oral cavity which may hinder wound healing.

In the wound healing process, administering tetracycline mouthwash has the ability to inhibit the activity of MMPs, where MMPs are always involved in the inflammatory process where platelets after biologically secrete active proteins that bind to the fibrin network and extracellular matrix (ECM), which initiates a chemotactic gradient and triggers the inflammatory phase in repair by recruiting inflammatory cells to the ulcer.<sup>10,11</sup> The wound healing process requires a decrease in the ECM and then progressive remodeling occurs to reach the maturation phase. The main enzymes involved in this degradation process are MMPs, which are a family with 24 differences that can work together to degrade ECM components.<sup>11</sup>

MMPs are divided into 4 subgroups based on their substrate specifications, namely: interstitial collagenases, stromelysins, type IV collagenases and membrane type-MMPs (MT-MMPs). All of them are secreted in a latent form which becomes biologically active and their activity is also tightly regulated by tissue inhibitors of metalloproteinases (TIMPs) which bind active MMP enzymes with high affinity.<sup>12</sup>

MMPs are produced by cells involved in wound healing including fibroblasts, keratinocytes and inflammatory cells. Its expression is modulated by response signals from cytokines, growth factors, cell-matrix interactions and changes in cell-cell contacts. The expression pattern of MMPs in normal wound healing is very complex and experiences changes in concentration based on the phases of the healing process. Apart from ECM remodeling patterns, MMPs have important functions including regulation and differentiation

of cell growth, in the wound healing process MMPs can change cell movement, influence interactions between cells, release growth factors and cytokines thereby influencing cell proliferation and growth.<sup>12</sup> Apart from that, MMPs also initiate debridement of devitalized tissue. MMPs are part of the inflammatory response and contribute to tissue damage in ulcers<sup>11,12</sup>, so administering tetracycline mouthwash in therapy as an inhibitor of MMPs activity (TIMPs) can help prevent excessive tissue debridement and actually damage tissue that is in the healing process.<sup>10</sup>

After using this tetracycline mouthwash, the patient felt more comfortable because the patient felt less pain than previously felt, the ulcer healing time was faster than the patient felt before and the ulceration did not continue to become larger. Tetracycline mouthwash 0.25% has the ability to reduce the feeling and duration of pain in ulcers, reduce severity by reducing the size of the ulcer, reduce the risk of secondary infection and inhibit collagenase.<sup>6,10</sup>

It is hoped that giving this multivitamin can help improve the patient's general condition to speed up the healing process. Vitamin A is required for differentiation and growth of epithelial tissue and improves immune system function. Vitamin B complex plays a role as a coenzyme in many biochemical reactions and carbohydrate metabolism in the body which ultimately helps speed up the human body's metabolism, increasing general body stamina. Vitamin C or ascorbic acid has an important role as a cofactor in the hydroxylation of proline residues for collagen synthesis. Vitamin C is also useful for maintaining connective tissue and helping connective tissue synthesis during healing.<sup>13</sup> Based on what has been explained above, it can be concluded that the main management of oral ulcers is to avoid allergen factors. Therapy with tetracycline mouthwash and multivitamins can reduce pain and speed up healing of ulcers in patients with a history of food allergies.

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